

REMARKS/ARGUMENTS

Claims 1, 3, 7, 8, 12-17 and 19 have been amended by way of this amendment. Claims 4-6, 9-11 and 20 have been cancelled, without prejudice or disclaimer. Claims 21 and 22 have been added. Claims 1-3, 7-8, 12-19 and 21-22 are pending in this application upon entry of these amendments.

The specification has been amended, as requested by the Examiner, to make proper reference to the International Application of which the present application is a national stage. No new matter has been added by way of this amendment.

Claim 1 has been amended to recite the phrase “a reporter gene,” rather than the phrase “ β -galactosidase reporter gene.” Support for this amendment can be found throughout the specification and in particular on page 3, lines 7-15 and line 26; page 5, lines 17 and 25; and page 6, lines 13-18.

Claims 1, 3, 8, and 12-17 have been amended to recite the phrase “HIV psi (ψ) sequence,” rather than “HIV psi (ψ) gene.” Support for this amendment can be found throughout the specification and, for example, on page 3, lines 15, 22, 25 and 34; page 8, line 22; and page 12, line 21.

Claims 1 and 12-17 have been amended to recite that the reporter gene is “located downstream of the HIV psi(ψ) sequence.” Support for this amendment can be found throughout the specification and in particular on page 5, lines 33-27; page 7, lines 28-35; page 8, lines 20-22; and Figure 1C.

Claim 3 has been amended to add the limitations of claims 4-6 in Markush form. Claim 8 has been amended to add the limitations of claims 9-11 in Markush form. In addition,

pNH1Psi(SL34) has been added to the Markush group of claim 8. Support for pNH1Psi(SL34) can be found throughout the specification and in particular in Table 1 (page 15), Figure 4 (see also description of Figure 4 on page 5, line 7), and page 13, lines 30-35 of the specification.

Claims 7 and 19 have been amended only to change the claim dependency.

Claims 21 and 22 have been added. Support for new claim 21 can be found throughout the specification and in particular on page 6, lines 13-18 and Figures 3a, 3b, and 4. Support for new claim 22 can be found throughout the specification and in particular, *e.g.*, on page 5, lines 23-28; page 6, lines 13-18; Example 1 (page 7, line 24 - page 9, line 17) and in originally filed claims 1, and 8-17.

No new matter has been added by way of these new claims or amendments.

35 U.S.C. § 120

As requested by the Examiner, the specification, by way of the present amendment, has been amended to indicate that the present application is a national stage entry of International Application No. PCT/KR00/01173, filed October 18, 2000.

35 U.S.C. § 119

The Examiner indicates in the Office Action that the foreign priority document (ROK 2000/0018489) is not on file. Attached at Exhibit 1 is a copy of Form PCT/IB/304 evidencing timely receipt of the priority document on November 7, 2000 during prosecution of corresponding International Application No. PCT/KR00/01173.

37 C.F.R. § 1.72

The Examiner has objected to the specification under 37 C.F.R. § 1.72(b) because the application allegedly does not contain an abstract. In order to comply with the requirements of 37 C.F.R. § 1.72(b), Applicants herein submit on a separate sheet entitled "Abstract" an abstract of the disclosure. This abstract corresponds to the abstract originally filed with the application on the first page of the application (i.e. on the bibliographic data page of the international application).

Rejection Under 35 U.S.C. §101

Claim 20 has been rejected for allegedly being directed to non-statutory subject matter.

Claim 20 has been cancelled, without prejudice or disclaimer. Accordingly, withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. §103(a)

Claims 1-20 have been rejected as allegedly obvious over Bacharach and Goff (J. Virol. 1998; herein "Bacharach") in view of Strair (Nucleic Acids Res 1993; herein "Strair"). The Examiner alleges that Bacharach discloses an assay for studying binding interactions between the HIV-1 nucleocapsid (NC) protein and HIV-1 psi (ψ) signal sequence and that the NC protein, target RNA, and reporter gene (β -gal) were expressed from separate plasmids. The Examiner further sets forth that Strair allegedly discloses a two-plasmid system for identifying

antivirals and drug-resistant variants. The Examiner concludes that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the screening assay of Bacharach to include the packaging signal and reporter gene on the same plasmid. The Examiner further alleges that numerous HIV-1 isolates have been sequenced and that selection of any packaging sequence and identification of suitable expression vectors would be a matter of routine experimentation.

This rejection is respectfully traversed. As acknowledged by the Examiner, Bacharach discloses a three-plasmid system for studying the interaction between the gag protein and psi. Nothing in Bacharach discloses or suggests that this system could be made into a simpler two-plasmid system, as disclosed and claimed in the present application. The Examiner cites Strair for providing a simpler two-plasmid system for developing antivirals. However, Strair does not disclose or suggest a simple two-plasmid system. Rather, Strair discloses a two-step system that is significantly more complicated than the presently claimed invention. Strair discloses a system in which two plasmids are transfected into COS cells to produce an HIV-lacZ virus. This HIV-lacZ virus is then transfected into a target cell and lacZ expression from this second cell is measured. Thus, the Strair system requires use of at least two cell populations and the production of viral particles to get a read-out from the reporter gene (*e.g.* β -galactosidase). In contrast with the Strair system, the presently claimed invention requires use of only one cell population and does not require the production of viral particles to get a read-out from the reporter gene (*e.g.* β -galactosidase). Thus, nothing in Bacharach or Strair teaches or discloses the simplified two-plasmid system of the present invention.

In addition to being simpler, the two-plasmid system of the present invention has other differences and advantages over the Bacharach three-plasmid and the Strair viral particle systems. For example, in the Bacharach and Strair systems, interaction of the viral protein (e.g. gag or NC) with the psi sequence results in transcription of the lacZ gene, while in the present invention such interaction results in downregulation of the expression of the lacZ gene. Thus, the presently claimed invention, unlike that of Bacharach and Strair, provides a system in which the direct interaction of the viral NC protein with psi results in downregulation of lacZ gene expression.

Additionally, the presently claimed system maintains the specificity of the interaction between the NC protein and the psi sequence, while that of Bacharach does not. Table 3 of Bacharach (on p. 6947 of Bacharach) demonstrates that in their system the specificity of NC-binding to psi is lost. For example, the NC protein of their system is capable of binding to haMSV and IRE. In contrast, the NC protein in the presently claimed system maintains its specificity for the HIV psi sequence (see Example 3 (page 12, lines 2-37 and page 13, lines 1-6) and Figure 3a). The Strair system does not allow for any specificity as the target of the antiviral drugs screened for in Strair is unknown. Thus, the presently claimed microorganism and methods of screening defined by the present claims allow for the interaction between the NC protein and psi to be tested, while the Bacharach or Strair techniques do not.

The present invention also provides a more sensitive screening system than that disclosed in Bacharach. Bacharach reports that the level of reporter gene expression is the same when NC or gag is used (see Table 3 of Bacharach). In contrast, the instant application demonstrates that the two-plasmid system results in different levels of reporter gene expression

when NC and gag are used (see Example 3 (page 13, lines 7-13) and Figure 3b of the instant application).

In conclusion, nothing in Bacharach or Strair suggests or discloses the presently claimed two-plasmid system or methods utilizing this two-plasmid system. In addition, to being simpler than the Bacharach and Strair systems, the present invention provides, as discussed above, several advantages over that of the Bacharach and Strair systems. Accordingly, the present invention is not obvious over Bacharach in view of Strair and Applicants respectfully request withdrawal of this rejection.

Conclusion

In view of the above amendments and remarks, it is respectfully requested that the application be reconsidered and that all pending claims be allowed and the case passed to issue. If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Respectfully submitted,

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Date of mailing (day/month/year) 15 November 2000 (15.11.00)	IMPORTANT NOTIFICATION
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International publication date (day/month/year) Not yet published	
Applicant YOU, Ji-Chang et al	International filing date (day/month/year) 18 October 2000 (18.10.00) Priority date (day/month/year) 08 April 2000 (08.04.00)

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<u>Priority date</u>	<u>Priority application No.</u>	<u>Country or regional Office or PCT receiving Office</u>	<u>Date of receipt of priority document</u>
08 April 2000 (08.04.00)	2000/0018489	KR	07 Nov 2000 (07.11.00)

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